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PII: S2352-5126(22)00138-2

DOI: https://doi.org/10.1016/j.jdcr.2022.03.011

Reference: JDCR 2292

To appear in: *JAAD Case Reports*

Received Date: 19 January 2022

Revised Date: 2 March 2022

Accepted Date: 6 March 2022

Please cite this article as: Bailly-Caillé B, Jouen F, Dompmartin A, Morice C, A Case Report of Anti-P200 Pemphigoid Following COVID-19 Vaccination, *JAAD Case Reports* (2022), doi: https://doi.org/10.1016/j.jdcr.2022.03.011.

Page de Titre:

Article type: case report

A Case Report of Anti-P200 Pemphigoid Following COVID-19 Vaccination

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Funding sources: no funding was received for this study.

Conflicts of interest: The authors have no conflict of interest to declare.

No prior presentation

Manuscript word count: 1000

Références: 9

Figures: 3 (in color)

Tables: 0

Informed consent

Informed consent: Written informed consent for publication of the clinical details was obtained from the participant.

Consent for publication: The participant provided consent for the submission of this case report to the journal.

Acknowledgements: The authors are grateful to Fabien Chaillot, Caen University Hospital, for his help in editing the manuscript.

Keywords: laminin γ1 (p200); anti-p200 pemphigoid; COVID-19 vaccination; trigger

Introduction

Anti-p200 pemphigoid is a rare autoimmune subepidermal bullous disease characterized by autoantibodies to laminin γ1 (p200). A few rare cases of autoimmune bullous dermatoses, mainly bullous pemphigoid, have been reported following COVID-19 vaccination.[1,2] Only one case of anti-p200 pemphigoid postvaccination has been reported after a pneumococcal vaccination.[3] We report a case of anti-p200 pemphigoid subsequent to COVID-19 vaccination.

Case Report

A 74-year-old man presented with sudden blisters of the extremities, hands, wrists, elbows, and feet, which appeared 48 hours after the second dose of the Moderna COVID-19 mRNA vaccine. A few vesicles located only on his wrists appeared 10 days after the first dose with spontaneous resolution. His medical history included eczema and glaucoma. No additional treatment had been initiated.

Physical examination revealed numerous tense and flaccid blisters on inflammatory skin, on the extremities (Figure 1A-D) and round erosion of the scrotum. Mucous membranes were unaffected. A local reaction site was also noted located at the injection area, with axillary lymphadenopathy. The patient did not have fever.

Laboratory evaluation showed only discrete biological inflammatory syndrome with a CRP of 44 mg/L without hyperleukocytosis. There was no hyper-eosinophilia. Histopathological examination showed subepidermal separation. Dermal infiltrate was composed of numerous eosinophils and few lymphocytes. Direct immunofluorescence revealed linear C3 and IgG deposition along the dermo epidermal junction (Figure 2). Indirect immunofluorescence of the patient sera on NaCl-split human skin showed IgG antibodies that were only bound to the dermal sides. Antibodies against BPAG-1, BPAG-2, and collagen VII were not detected by ELISA. Immunoblot analysis of human dermal extracts revealed IgG4 that recognized a 200-kDa band corresponding to anti-p200 antibodies (Figure 3). A diagnosis of anti-p200 pemphigoid was established. The workup results for malignancy and for other autoimmune diseases conducted by a computed tomographic scan and laboratory test were negative.

The patient was initially treated with topical corticosteroids by Clobetasol propionate 0,05% cream with a transient effect. New lesions appeared during the decrease in topical corticosteroids. Colchicine (1 mg/day) and daily application of a topical corticosteroid led to a significant improvement after a delay of 15 days. Colchicine was stopped after 2 months because of hepatic cholestasis, and the use frequency of the topical corticosteroid was decreased over 4 months. Remission was sustained for 6 months after the treatment.

Discussion

A broad spectrum of cutaneous adverse events has been described after mRNA COVID-19 vaccination, including subepidermal bullous disease such as bullous pemphigoid (BP). The most frequently reported adverse effects were local injection site reactions, urticaria, morbilliform rashes, and pityriasis rosea-like reactions.[2,4] It seems that after the second dose, less than 50% relapse.[5]

Some cases of BP following COVID-19 vaccination have been described recently, highlighting the potential triggering role of the mRNA COVID-19 vaccine in autoimmune subepidermal bullous disease initiation. Our anti-p200 pemphigoid case seems to be different from other BP cases not only by these features but also by its evolution. Indeed, the majority of described BP following COVID-19 vaccination began after the second dose with a median onset on Day 7.[1] In our clinical case, we noticed the first eruption 10 days after the first dose, with a more intense and rapid relapse after the second dose, and remission after 6 months, corresponding with a decrease in COVID-19-specific antibodies following immunization. The close temporal relationship between vaccination and the onset of anti-p200 pemphigoid in our patient reinforced the potential triggering role of the COVID-19 vaccine.

We suggest that vaccination may be the triggering factor of autoimmune subepidermal bullous diseases by stimulating the immune system with an unexplained mechanism. Indeed, vaccination could unmask subclinical disease defined by the presence of antibodies before clinical symptoms[6] through the immunostimulatory process of the vaccine and initiate rapid lesions after the first dose. In patients with more delayed kinetics, it could reflect a period of antibody production. COVID-19 vaccination is the first use of mRNA vaccines in humans and additional studies will be needed to understand the

potential role of COVID-19 vaccination in initiating the development of autoimmune subepidermal bullous diseases.

Epidermolysis bullosa acquisita should be considered in the differential diagnosis, which was ruled out thanks to immunoblot and by lack of autoantibodies targeting type VII collagen. The diagnosis of anti-p200 pemphigoid can be challenging, as it shares clinical and histopathologic characteristics with other blistering diseases. Some cases of anti-p200 pemphigoid closely looked like epidermolysis bullosa acquisita, with lesions on extremities. Mucosal involvement was also described. Patients are younger than those with bullous pemphigoid. Detection of autoantibodies recognizing a 200-kD protein by immunoblotting of human dermal extract, corresponding to laminin γ1, confirmed the diagnosis.[7]

Of the 12 cases of bullous eruption following COVID-19 vaccination described by Tomayko et al.,[1] 3 had negative immunologic testing. Nevertheless, detection of anti-p200 antibodies was not performed, possibly underestimating the cases of anti-p200 pemphigoid, as it resembles bullous pemphigoid. Specific research on the anti-p200 antibody must be realized to avoid being unware of the diagnosis of anti-p200 pemphigoid.

In this same series of 12 patients reported by Tomayko et al.,[1] the clinical course was variable. The authors suggest that these different developments may reflect different pathophysiological mechanisms: BP-like disease and BP unmasked by vaccination, which require stronger treatment.

Anti-p200 pemphigoid is usually a chronic disease, with a more severe and relapsing course than BP despite the use of systemic treatment.[3,7] In our case, systemic treatment with colchicine was required, combined with a topical corticosteroid due to the recurrent course. Complete remission was obtained for 6 months despite the discontinuation of colchicine after 2 months of treatment due to the appearance of hepatitis cholestasis.

Cases of disease flare were described following vaccination during a period of remission in patients with BP.[8] In our case, a worsening of the lesions appeared after the second dose.

In conclusion, this rare autoimmune bullous disease can be induced or revealed by the Moderna COVID-19 mRNA vaccine. For this specific patient, another dose of the vaccine may be accompanied by a risk of relapse of the dermatosis. The risk-benefit ratio must be carefully assessed with the patient.[8,9]

Conflict of Interest Disclosures: None reported.

Abbreviation used: BP: bullous pemphigoid; mRNA: messenger RNA

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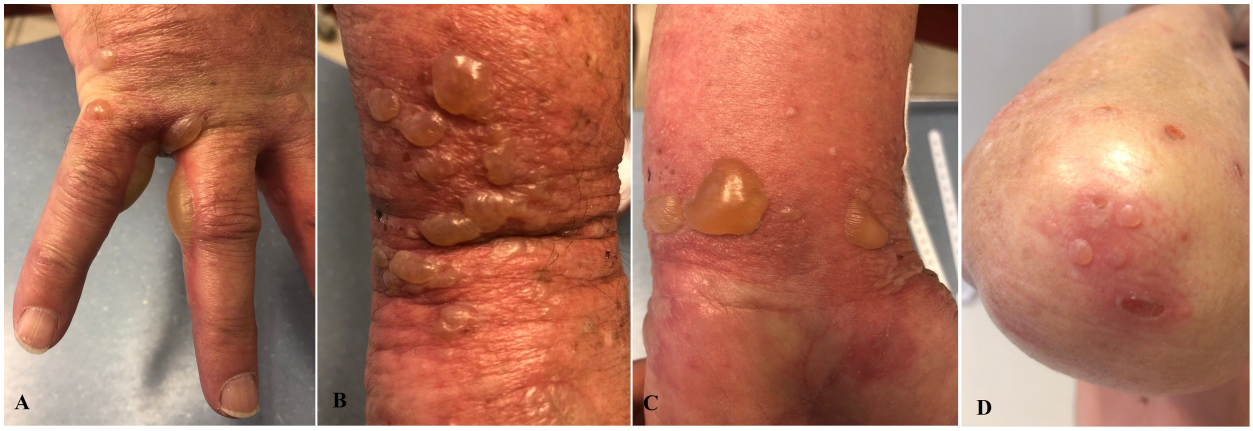
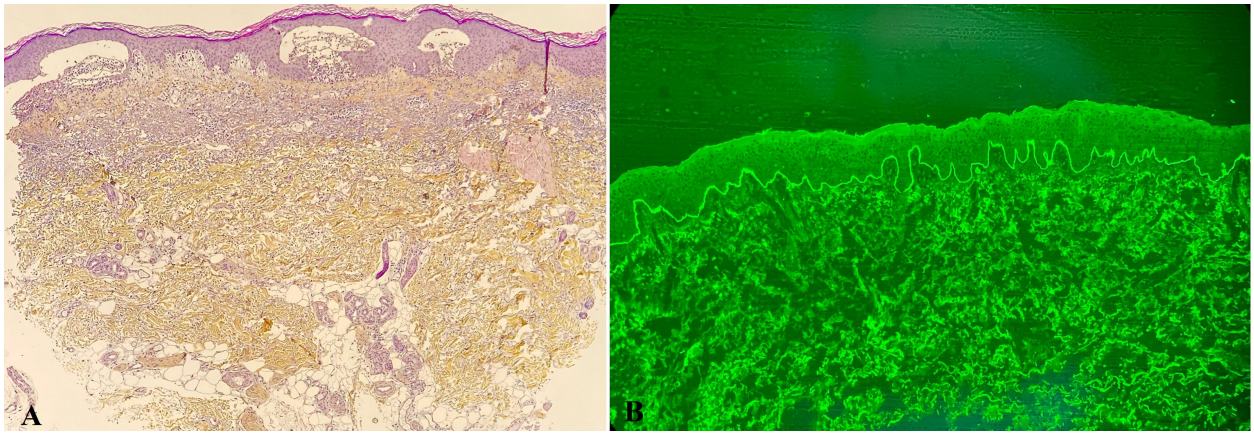
Figure legends

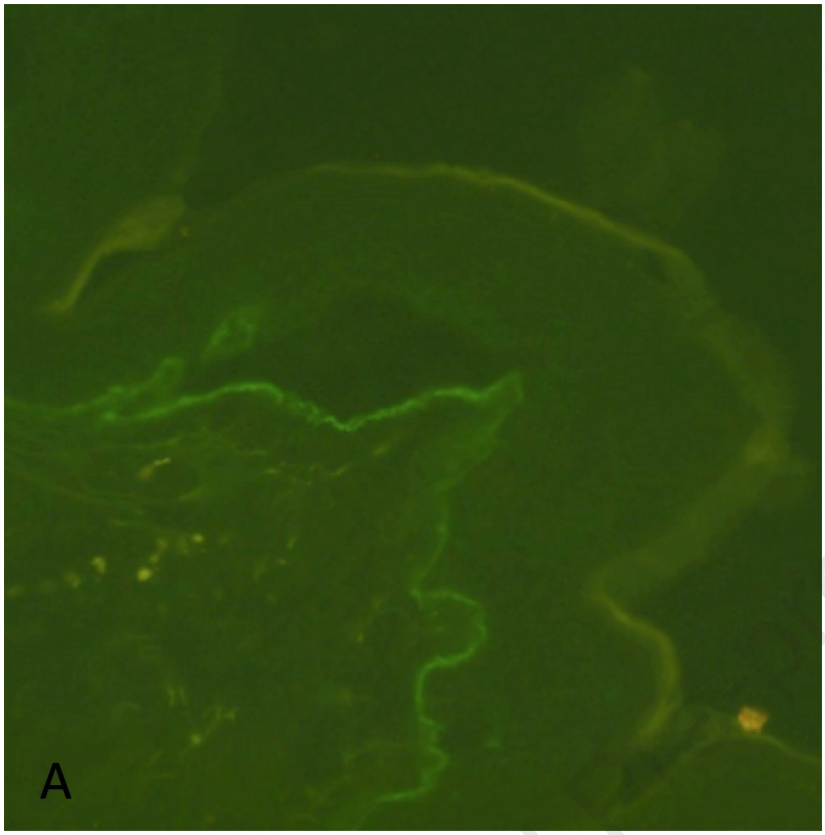
Figure 1. Clinical features of the wrist (A-B), lateral side of the fingers (C), and elbow (D).

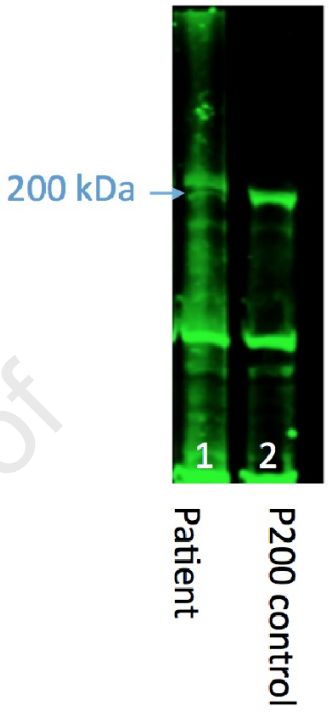
Figure 2. Histopathological findings. A: Subepidermal blistering with dermal infiltrate with numerous eosinophils. Haematoxylin-eosine stained section. B: Immunofluorescence direct.

Figure 3. A: Indirect immunofluorescence using salt-split skin showed bound immunoglobulin IgG on the dermal side. B: Immunoblotting with dermal extracts confirmed that the patient's IgG autoantibodies reacted with a 200-kDa protein.









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